

## **REMARKS**

Claims 1-96 are under examination.

Applicants are hereby affirming the provisional election made on March 9, 2006 to prosecute Group I (claims 1-11, 18-20, 32-38, 40-48, 53, 54 and 63-69).

Claims 12-17, 21-31, 39, 49-52, 55-62 and 70-96 have been withdrawn as being drawn to non-elected inventions. Applicants reserve the right to file divisional applications on all non-elected subject matter of the instant application. Claims 1, 3-10, 18, 19, 32-38, 40, 42-48, 53, 54, 63 and 65-69 have been amended. Claims 2, 41 and 64 have been cancelled.

### **Objections**

To the Abstract:

The abstract of the disclosure stands objected as not conveying structural makeup (page 6, 2<sup>nd</sup> paragraph of Office Action). Applicants have amended the specification by providing the Abstract that includes definition of the variables in formula (I). Applicants respectfully request the objection be removed.

To the claims:

Claim 5 stands objected under 37 CFR 1.75(c) for failing to further limit the subject matter of a previous claim (page 7, 3<sup>rd</sup> paragraph of Office Action). Applicants respectfully traverse. Claim 4 discloses a compound of formula (I) wherein R<sub>2</sub> is an aryl group selected from the group consisting of naphthyl and phenyl wherein the phenyl is substituted with 0, 1 or 2 substituents independently selected from the group consisting of alkyl, cyano and halogen. Claim 5 recites specific species and is clearly a subset of claim 4. Applicants maintain that claim 5 further limits the subject matter of claim 4 and is a proper dependent claim of claim 4. Therefore, Applicants respectfully request the Examiner to reconsider and withdraw this objection.

Claims 8, 11 and 20 are objected to as being dependent upon a rejected base claim (page 12, 2<sup>nd</sup> paragraph of Office Action). The base claims of each of the objected claims have been amended.

Applicants respectfully submit that all objections have been properly addressed and request their withdrawal.

Claim Rejections – 35 USC § 101

Claim 5 stands rejected for lack of patentability (page 8, 1<sup>st</sup> paragraph of Office Action). Specifically, the examiner stated that the 4<sup>th</sup> and 7<sup>th</sup> “dioxime” species on p.143 are outside the generic formula. Applicants have deleted the two “dioxime” species from claim 5 and respectfully request the withdrawal of the rejection.

Claim Rejections – 35 USC § 112 second paragraph

Claims 1-4, 6, 7, 9, 10, 18, 19, 32-38, 40-43, 45-48, 53, 54, 63-69 are rejected under 35 U.S.C. 112, second paragraph (page 6, 3<sup>rd</sup> paragraph of Office Action). The Examiner noted that the specification does not provide guidelines for the type of prodrugs suitable for the invention. Applicants have deleted the terms “prodrugs” from claims 1, 33-38, 40, and 65-69. Claims 3, 4, 6, 7, 9, 10, 18, 19, 42, 45-48, 53, 54 are dependent claims. Claims 2, 41, and 64 have been cancelled. Claims 32 and 63 are directed to pharmaceutical compositions comprising compounds of the instant invention in combination with a therapeutically acceptable carrier.

Claims 32-38 and 63-69 are rejected to as incomplete independent claims. Applicants have amended claims 32-38, and 63-69 to make them dependent upon claims 1 and 40, respectively.. Claim 64 has been cancelled.

Applicants respectfully submits that, in view of the amendments, the rejections are now moot and request their withdrawals.

Claim Rejections – 35 USC § 112 first paragraph

Claims 1-4, 6, 7, 9, 10, 18, 19, 32-38, 40-48, 53, 54 and 63-69 stand rejected under 35 USC § 112 first paragraph (page 8, 2<sup>nd</sup> paragraph of Office Action) as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which is most nearly connected, to make and/or use the invention. Specifically the Examiner maintains that the specification does not enable one skilled in the art to know whether all classes of known prodrugs will

have the ability to regenerate *in vivo* to the instant compounds by one or more biological processes. Applicants have deleted the terms “prodrugs” from claims 1, 33-38, 40 and 65-69. Claims 2, 41 and 64 have been cancelled. Claims 3, 4, 6, 7, 9, 10, 18, 19, 42-48, 53 and 54 are dependent claims. Claim 32 and 63 are directed to pharmaceutical compositions comprising compounds of the instant invention in combination with a therapeutically acceptable carrier and do not contain the language of prodrug. Claim 64 has been cancelled. Applicants respectfully request that in view of the amendments , the rejection be withdrawn.

The Examiner rejected Claims 1-4, 6, 7, 9, 10, 18, 19, 32-38, 40-48, 53, 54 and 63-69 under 35 USC § 112 first paragraph as the scope at R<sub>2</sub> and R<sub>4</sub> as heteroaryl is not adequately enabling (page 9, 2<sup>nd</sup> paragraph). Applicants respectfully traverse the rejection. The combination of R<sub>2</sub> and R<sub>4</sub> as heteroaryl does not cover “millions of compounds”. Applicants have also provided descriptions and data in the specification so that one ordinary skilled in the art can make and use the invention without undue experimentation. Applicants submit that the range provided was obtained from the results of 85 out of the 100 compounds that were tested for both *in vitro* and *in vivo* activity. Applicants can provide the correlation tables for the biological activity of the compounds tested if the Examiner so require. To expedite prosecution, applicants have amended claims 1, 32-38, 40, 63, and 65-69 to include heteroaryl rings that are monocyclic, five or six membered rings containing 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, O, and S. Claims 3, 4, 6, 7, 9, 10, 18, 19, 42-48, 53 and 54 are dependent claims. Claims 2, 41 and 64 have been cancelled. Accordingly, Applicants respectfully request the withdrawal of the rejection.

Claims 1-3, 6, 9, 18, 32 – 38, 40-42, 45, 47 and 63-69 are rejected as not enabled given the current state of the art in the dopamine area (page 10, last 2 paragraphs of Office Action) Examiner sustains that the method claims that cover all forms of male and female sexual dysfunction are not adequately enabled. Applicants respectfully traverse the rejection. The present invention relates to the use of specific dopamine agonists acting selectively on D<sub>4</sub> dopamine receptors that are located in specific areas of the CNS. As stated in the description of the present application, these areas i.e., medial preoptic area of the hypothalamus (MPOA) and the paraventricular nucleus (PVN) are known to

have a critical role in animal sexual behavior. Since there is no evidence that the localization of the D4 dopamine receptors varies with gender, there is no reason to assume that compounds that affect the sexual behavior of male mammals would not affect the sexual behavior of female mammals. Additionally, the relevant law states that to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must teach one of skill in the art to make and use the invention without undue experimentation. This requirement can be satisfied by providing sufficient disclosure, either through illustrative examples or broad terminology. This clause does not require “a specific example of everything *within the scope* of a broad claim”. In re Anderson 176 USPQ 331, at 333 (CCPA 1973). The inquiry with respect to scope of enablement under 35 U.S.C. § 112, first paragraph is whether it would require undue experimentation to make and use the claimed invention. A considerable amount of experimentation is permissible, particularly if it is routine experimentation. The effect of the compounds of the present invention was tested in the rat penile erectile model , which is widely recognized as an effective model to test compounds that would affect sexual behavior in general. Therefore, Applicants respectfully request the Examiner to reconsider and withdraw the rejection.

Rejection under 35 U.S.C. § 102(b)

Claims 1-4, 32 and 63 are rejected under 35 U.S.C. § 102(b) as being anticipated by Buzas (GB'523; page 11, 2<sup>nd</sup> paragraph of Office Action). The reference teaches compounds wherein instant L is -(CH<sub>2</sub>)<sub>3</sub>-, R<sub>1</sub> is allyl, R<sub>2</sub> is 4-fluorophenyl, R<sub>3</sub> is piperazinyl and R<sub>4</sub> is 2-pyridinyl, . Claims 1-4 of the present invention are directed compounds wherein L is C<sub>1</sub>-C<sub>2</sub> alkylene, R<sub>2</sub> is heteroaryl, R<sub>3</sub> is piperazinyl, and R<sub>4</sub> is heteroaryl. Claim 32 is directed to pharmaceutical composition comprising compounds of the invention in combination with a therapeutically acceptable carrier. In order for a reference to anticipate an invention, that reference must recite each and every element of the claimed invention. Applicants respectfully submit that Buzas (GB'523) fails to meet this legal requirement in relation to claims 1-4 and 32. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1-4 and 32. Claim 63 is amended to include a pharmaceutical composition comprising compounds of formula (Ia)

in combination with a therapeutically acceptable carrier, wherein R<sub>1</sub> is selected from the group consisting of hydrogen, alkoxyalkyl, alkyl, alkynyl, arylalkyl, cyanoalkyl, cycloalkyl, haloalkyl, and hydroxyalkyl. The rejection of claim 63 under 35 U.S.C. § 102(b) as being anticipated by Buzas (GB'523) is now moot in view of the amendment. Accordingly, Applicants respectfully request withdrawal of the rejection of claim 63

Rejection under 35 U.S.C. § 103(a)

Claim 5 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Buzas (GB '523) (page 12, 1<sup>st</sup> paragraph of Office Action). Examiner notes that the 5<sup>th</sup> and 6<sup>th</sup> species on p.141 and 7<sup>th</sup>-8<sup>th</sup> species on p. 142 of claim 5 of instant application are obvious variants over the species disclosed in the cited reference. GB '523 teaches compounds wherein R<sub>1</sub> is allyl, R<sub>2</sub> is 4-fluorophenyl, R<sub>3</sub> is piperazinyl, R<sub>4</sub> is pyridinyl and L is C<sub>3</sub> alkylene. Examiner also notes that GB '523 teaches lower aliphatic groups as suitable choices at instant R<sub>1</sub> and instant "L" can be 1 to 3 carbons chain. Examiner then asserts that it would have been obvious to one skilled in the art at the time the instant invention was made to modify the species in Buzas by altering the chain length corresponding to instant "L" as well as modifying the aliphatic group in instant R<sub>1</sub> to obtain the compounds of the present invention.with the expectation that resulting compounds will also posses the uses taught by Buzas.

To establish *prima facie* obviousness, the Examiner must identify, from a source other than Applicants' own specification both *a suggestion* to modify a primary reference to achieve the presently claimed invention and *a reasonable expectation of success* in making and using the modified procedure to obtain the compounds of the present application useful to treat sexual dysfunction. The modification must be more than just "obvious to try", which has been rejected by the courts as a standard for obviousness (see e.g. In re O'Farrell, 7 USPQ2d 1673 (Fed. Cir. 1988)). Under these standards, Applicants respectfully contend that Buzas (GB'523) fails to render Applicant's invention obvious.

Conclusions

In view of the amendments and the aforementioned remarks, Applicants respectfully believe that the application is in condition for allowance and respectfully request that the Examiner withdraw all outstanding rejections and passes this application to allowance.

Should the Examiner have any concerns regarding the above, he is respectfully requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,  
T. Kolasa, et al.



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